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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,880	05/14/2001	Gregory J. Riggins	00250.00003	6566

22907 7590 12/15/2004

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WASHINGTON, DC 20001

EXAMINER

YAEN, CHRISTOPHER H

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 12/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/853,880

Applicant(s)

RIGGINS ET AL.

Examiner

Christopher H Yaen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13, 16 and 18-22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13, 16 and 18-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Re: Riggins GJ et al
Priority Date: 14 May 2001

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/30/2004 has been entered.
2. Accordingly, claims 1-12,14-15,17,24-47 are canceled without prejudice or disclaimer.
3. Claims 13,16, and 18-22 are pending and examined on the merits.
4. The declaration filed on 3/30/2004 by G. J. Riggins is acknowledged and considered.
5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Maintained - 35 USC § 112, 1st paragraph

6. The rejection of claims 13,16,18-22 under 35 USC § 112,1st paragraph as lacking an enabling disclosure is maintained for the reasons of record. Applicant argues that the enablement rejection set forth is "legally insufficient" and further states that the

specification need not contain an example if the invention can be practice by one of skill in the art without undue experimentation (see page 5 of response filed 3/30/2004).

Applicant further argues by analyzing the instant invention using the 8 factors outlined under *In re Wands* (see page 5-8). In particular, applicant points out that the prior art provides the skilled artisan with many examples of antibody conjugates that are capable of targeting cancers and that such antibody conjugates are useful in diagnostic or therapeutic applications (see page 6-8). Applicant also points out that because the prior art teaches immunoconjugates and that such immunoconjugates can reach the intended target, the only difference between the instant invention and that already provided in the prior art is the target. Applicant concludes by stating that the nature of the invention is that it is a different version of similar technology. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

The claims are drawn to a method of specifically delivering a reagent to a glioblastoma comprising contacting cells of a glioblastoma with an antibody which is conjugated with a reagent, wherein the antibody specifically binds to SEQ ID No: 17. Subsequent claims are drawn to the nature of the glioblastoma (claim 16), the types of reagents conjugated to the antibody (claims 18-21) and location of the glioblastoma (claim 22). The specification teaches that through SAGE analysis several genes are up-regulated when compared to normal tissue. In particular, the specification teaches that amongst the genes that are up regulated is GPNMB (i.e. SEQ ID No: 17). Aside from referencing GPNMB by gene accession number (see page 26), the specification

provides little guidance in terms of what the protein is, how it functions, or whether the expression of the protein is correlative with the up-regulation of its RNA. The specification does however incorporate by reference a reference by Weterman *et al* which discusses the discovery of the *nmb* gene and the appearance of the *nmb* gene product on the surface of the cell when artificially expressed in a cell. However, aside from this teaching, the specification does not provide one of skill in the art with any indication that the method of specifically delivering a reagent to a tumor that is located within the brain can be practiced without undue experimentation.

Although the art does teach many methods of delivering reagents conjugated to antibodies to specific targets, as argued by the applicant, there is to some extent a degree of unpredictability associated with the delivery of reagents conjugated to antibodies to tumors. For example, Curti (Clinical Reviews in Oncology/Hematology 1993;14:29-39) teaches that once a therapeutic agent is administered to a subject there are several "spaces with different physiological characteristics" that must be traversed, among them include the vascular endothelium and tumor interstitium. Finally Curti concludes by asking the question "does the treatment get to the tumor?" In another example, Jain (Science 1996; 271:1079-1080) discusses the physical barriers that must be overcome prior to the delivery of "magic bullets" which he characterizes as antibodies, cytokines, antisense, oligonucleotides, gene vectors, and genetically engineered cells. Jain indicates that despite the advances in the development of these "magic bullets", more work and investigation is required in understanding the pathophysiology of solid tumors so that the "magic bullets" can be more effectively

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delivery to the tumors. Moreover, the majority of the prior art references presented by the applicant are not commensurate in scope to the claims because applicants are comparing known tumor associated antigens to the instant invention. The assertion of the instant protein as a tumor associated antigen is speculative at best. Applicant also indicates that in "Embodiments 2A-2D describe data which demonstrates the GPNMB is glioblastoma specific", and further indicates that the actual data is presented by Logging *et al* (see page 9-10 of response). However, upon closer inspection of the record, no such reference can be found to indicate that the instant GPNMB protein is actually a tumor specific marker for glioblastoma. Thus in the absence of evidence to indicate the instant protein is indeed differentially expressed in glioblastoma versus normal, and in the absence of any indication of protein expression, one of skill is left to experiment.

Thus despite the exemplification of working immunocojugates in the field, the need for working examples in this particular instance are required because it appears to be highly unpredictable whether the antibody is capable of reaching its intended target and if so, whether it is capable of eliciting any effect.

Therefore the rejection under 35 USC 112, 1st paragraph as lacking an enabling disclosure is maintained for the reasons of record.

It is noted that the rejection of claims under 35 USC 112, 1st paragraph as lacking an enabling disclosure specifically regarding the accession number of the GPNMB gene is withdrawn.

Conclusion

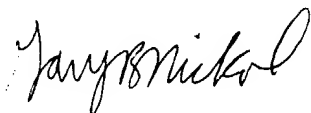
No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1642
December 6, 2004



GARY NICKOL
PRIMARY EXAMINER